FORM LG-4878

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E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED
WILMINGTON, DELAWARE 19898

LEGAL DEPARTMENT

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8EHQ-T2-12146
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Office of Pollution Prevention and Toxics
Environmental Protection Agency
401 M Street., S.W.
Washington, D.C. 20460
Attn: Section 8(e) Coordinator (CAP Agreement)

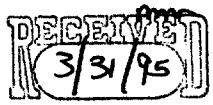
Dear Coordinator:

8ECAP-0025

On behalf of the Regulatee and pursuant to Unit II B.1.b. and Unit II C of the 6/28/CAP Agreement, E.I. Du Pont de Nemours and Co. hereby submits (*in triplicate*) the attached studies. Submission of this information is voluntary and is occasioned by unilateral changes in EPA's standard as to what EPA now considers as reportable information. Regulatee's submission of information is made solely in response to the new EPA §8(e) reporting standards and is not an admission: (1) of TSCA violation or liability; (2) that Regulatee's activities with the study compounds reasonably support a conclusion of substantial health or environmental risk or (3) that the studies themselves reasonably support a conclusion of substantial health or environmental risk.

For Regulatee,

Mark H. Christman
Counsel
Legal D-7058
1007 Market Street
Wilmington, DE 19898
(302) 774-6443



## ATTACHMENT 1

Submission of information is made under the 6/28/91 CAP Agreement, Unit II. This submission is made voluntarily and is occasioned by recent changes in EPA's TSCA §8(e) reporting standard; such changes made, for the first time in 1991 and 1992 without prior notice and in violation of Regulatee's constitutional due process rights. Regulatee's submission of information under this changed standard is not a waiver of its due process rights; an admission of TSCA violation or liability, or an admission that Regulatee's activities with the study compounds reasonably support a conclusion of substantial risk to health or to the environment. Regulatee has historically relied in good faith upon the 1978 Statement of Interpretation and Enforcement Policy criteria for determining whether study information is reportable under TSCA §8(e), 43 Fed Reg 11110 (March 16, 1978). EPA has not, to date, amended this Statement of Interpretation.

After CAP registration, EPA provided the Regulatee the June 1, 1991 "TSCA Section 8(e) Reporting Guide". This "Guide" has been further amended by EPA, EPA letter, April 10, 1992. EPA has not indicated that the "Reporting Guide" or the April 1992 amendment supersedes the 1978 Statement of Interpretation. The "Reporting Guide" and April 1992 amendment substantively lowers the Statement of Interpretation 's TSCA §8(e) reporting standard[2]. This is particularly troublesome as the "Reporting Guide" states criteria, applied retroactively, which expands upon and conflicts with the Statement of Interpretation.[3] Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" and the April 1992 amendment clouds the appropriate standard by which regulated persons must assess information for purposes of TSCA §8(e).

Throughout the CAP, EPA has mischaracterized the 1991 guidance as reflecting "longstanding" EPA policy concerning the standards by which toxicity information should be reviewed for purposes of §8(e) compliance. Regulatee recognizes that experience with the 1978 Statement of Interpretation may cause a review of its criteri. Regulatee supports and has no objection to the Agency's amending reporting criteria *provided that* such amendment is not applied to the regulated community in an unfair way. However, with the unilateral announcement of the CAP under the auspices of an enforcement proceeding, EPA has wrought a terrific unfairness since much of the criteria EPA has espoused in the June 1991 Reporting Guide and in the Agency's April 2, 1992 amendment is new criteria which does not exist in the 1978 Statement of Interpretation and Enforcement Policy.

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[2]In sharp contrast to the Agency's 1977 and 1978 actions to soliciting public comment on the proposed and final §8(e) Policy, EPA has unilaterally pronounced §8(e) substantive reporting criteria in the 1991 Section 8(e) Guide without public notice and comment, See 42 Fed Reg 45362 (9/9/77), "Notification of Substantial Risk under Section 8(e): Proposed Guidance".

[3]A comparison of the 1978 Statement of Interpretation and the 1992 "Reporting Guide" is a appended.

The following examples of new criteria contained in the "Reporting Guide" that is not contained in the Statement of Interpretation follow:

- even though EPA expressly disclaims each "status report" as being preliminary evaluations that should not be regarded as final EPA policy or intent[4], the "Reporting Guide" gives the "status reports" great weight as "sound and adequate basis" from which to determine mandatory reporting obligations. ("Guide" at page 20).
- the "Reporting Guide" contains a matrix that establishes new numerical reporting "cutoff" concentrations for acute lethality information ("Guide" at p. 31). Neither this matrix nor the cutoff values therein are contained in the Statement of Interpretation. The regulated community was not made aware of these cutoff values prior to issuance of the "Reporting Guide" in June, 1991.
- the "Reporting Guide" states new specific definitional criteria with which the Agency, for the first time, defines as 'distinguishable neurotoxicological effects'; such criteria/guidance not expressed in the 1978 Statement of Interpretation.[5];

- the "Reporting Guide" provides new review/ reporting criteria for irritation and sensitization studies; such criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy.
- the "Reporting Guide" publicizes certain EPA Q/A criteria issued to the Monsanto Co. in 1989 which are not in the Statement of Interpretation; have never been published in the Federal Register or distributed by the EPA to the Regulatee. Such Q/A establishes new reporting criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy .

In discharging its responsibilities, an administrative agency must give the regulated community fair and adequate warning to as what constitutes noncompliance for which penalties may be assessed.

> Among the myriad applications of the due process clause is the fundamental principle that statutes and regulations which purport to govern conduct must give an adequate warning of what they command or forbid.... Even a regulation which governs purely economic or commercial activities, if its violation can engender penalties, must be so framed as to provide a constitutionally adequate warning to those whose activities are governed.

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[4]The 'status reports' address the significance, if any, of particular information reported to the Agency, rather than stating EPA's interpretation of §8(e) reporting criteria. In the infrequent instances in which the status reports contain discussion of reportability, the analysis is invariably quite limited, without substantial supporting scientific or legal rationale.

[5] *See, e.g.* 10/2/91 letter from Du Pont to EPA regarding the definition of 'serious and prolonged effects' as this term may relate to transient anesthetic effects observed at lethal levels; 10/1/91 letter from the American Petroleum Institute to EPA regarding clarification of the Reporting Guide criteria.

Diebold, Inc. v. Marshall, 585 F.2d 1327, 1335-36 (D.C. Cir. 1978). *See also*, Rollins Environemntal Services (NJ) Inc. v. U.S. Environmental Protection Agency, 937 F. 2d 649 (D.C. Cir. 1991).

While neither the are rules, This principle has been applied to hold that agency 'clarification', such as the Statement of Interpretation, the "Reporting Guide" nor the April 1992 amendments will not applied retroactively.

> ...a federal court will not retroactively apply an unforeseeable interpretation of an administrative regulation to the detriment of a regulated party on the theory that the post hoc interpretation asserted by the Agency is generally consistent with the policies underlying the Agency's regulatory program, when the semantic meaning of the regulations, as previously drafted and construed by the appropriate agency, does not support the interpretation which that agency urges upon the court.

Standard Oil Co. v. Federal Energy Administration, 453 F. Supp. 203, 240 (N.D. Ohio 1978), aff'd sub nom. Standard Oil Co. v. Department of Energy, 596 F.2d 1029 (Em. App. 1978):

The 1978 Statement of Interpretation does not provide adequate notice of, and indeed conflicts with, the Agency's current position at §8(e) requires reporting of all 'positive' toxicological findings without regard to an assessment of their relevance to human health. In accordance with the statute, EPA's 1978 Statement of Interpretation requires the regulated community to use scientific judgment to evaluate the significance of toxicological findings and to determining whether they reasonably support a conclusion of a substantial risk. Part V of the Statement of Interpretation urges persons to consider "the fact or probability" of an effect's occurrence. Similarly, the 1978 Statement of Interpretation stresses that an animal study is reportable only when "it contains reliable evidence ascribing the effect to the chemical." 43 Fed Reg. at 11112. Moreover, EPA's Statement of Interpretation defines the substantiality of risk as a function of both the seriousness of the effect and the probability of its occurrence. 43 Fed Reg 11110 (1978). Earlier Agency interpretation also emphasized the "substantial" nature of a §8(e) determination. See 42 Fed Reg 45362, 45363 (1977). [Section 8(e) findings require "extraordinary exposure to a chemical substance...which critically imperil human health or the environment"].

The recently issued "Reporting Guide" and April 1992 Amendment guidance requires reporting beyond and inconsistent with that required by the Statement of Interpretation. Given the statute and the Statement of Interpretation's explicit focus on substantial human or environmental risk, whether a substance poses a "substantial risk" of injury requires the application of scientific judgment to the available data on a case-by-case basis.

If an overall weight-of-evidence analysis indicates that this classification is unwarranted, reporting should be unnecessary under §8(e) because the available data will not "reasonably support the conclusion" that the

chemical presents a substantial risk of serious adverse consequences to human health.

Neither the legislative history of §8(e) nor the plain meaning of the statute support EPA's recent lowering of the reporting threshold that TSCA §8(e) was intended to be a sweeping information gathering mechanism. In introducing the new version of the toxic substances legislation, Representative Eckhart included for the record discussion of the specific changes from the version of H. R. 10318 reported by the Consumer Protection and Finance Subcommittee in December 1975. One of these changes was to modify the standard for reporting under §8(e). The standard in the House version was changed from "causes or contributes to an unreasonable risk" to "causes or significantly contributes to a substantial risk". This particular change was one of several made in TSCA §8 to avoid placing an undue burden on the regulated community. The final changes to focus the scope of Section 8(e) were made in the version reported by the Conference Committee.

The word "substantial" means "considerable in importance, value, degree, amount or extent". Therefore, as generally understood, a "substantial risk" is one which will affect a considerable number of people or portion of the environment, will cause serious injury and is based on reasonably sound scientific analysis or data. Support for the interpretation can be found in a similar provision in the Consumer Product Safety Act. Section 15 of the CPSA defines a "substantial product hazard" to be:

> "a product defect which because of the pattern of defect, the number of defective products distributed in commerce, the severity of the risk, or otherwise, creates a substantial risk of injury to the public."

Similarly, EPA has interpreted the word 'substantial' as a quantitative measurement. Thus, a 'substantial risk' is a risk that can be quantified, *See*, 56 Fed Reg 32292, 32297 (7/15/91). Finally, since information pertinent to the exposure of humans or the environment to chemical substances or mixtures may be obtained by EPA through Sections 8(a) and 8(d) regardless of the degree of potential risk, §8(e) has specialized function. Consequently, information subject to §8(e) reporting should be of a type which would lead a reasonable man to conclude that some type action was required immediately to prevent injury to health or the environment.

# APPENDIX

*Comparison:* Criteria found in the 1978 "Statement of Interpretation/ Enforcement Policy", 43 Fed Reg 11110 (3/16/78) and the June 1991 Section 8(e) Guide.

| TOXICITY TEST TYPE | 1978 POLICY CRITERIA EXIST? | New 1991 GUIDE CRITERIA EXIST? |
|---|---|---|
| **ACUTE LETHALITY** | | |
| Oral | N} | Y} |
| Dermal | N} | Y} |
| Inhalation (Vapors) | }[1] | }[2] |
| aerosol | N} | Y} |
| dusts/ particles | N} | Y} |
| **SKIN IRRITATION** | N | Y[3] |
| **SKIN SENSITIZATION** | N | Y[4] |
| **EYE IRRITATION** | N | Y[5] |
| **SUBCHRONIC (ORAL/DERMAL/INHALATION)** | N | Y[6] |
| **REPRODUCTION STUDY** | N | Y[7] |
| **DEVELOPMENTAL TOX** | Y[8] | Y[9] |

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[1] 43 Fed Reg at 11114, comment 14:
"This policy statements directs the reporting of specified effects when unknown to the Administrator. Many routine tests are based on a knowledge of toxicity associated with a chemical unknown effects occurring during such a range test may have to be reported if they are those of concern tot he Agency and if the information meets the criteria set forth in Parts V and VII."

[2] Guide at pp.22, 29-31.

[3] Guide at pp-34-36.

[4] Guide at pp-34-36.

[5] Guide at pp-34-36.

[6] Guide at pp-22; 36-37.

[7] Guide at pp-22

[8] 43 Fed Reg at 11112
Only the term "Birth Defects" is listed.

| | | |
|---|---|---|
| **NEUROTOXICITY** | N | Y[10] |
| **CARCINOGENICITY** | Y[11] | Y[12] |
| **MUTAGENICITY** | | |
| *In Vitro* | Y][13] | Y] [14] |
| *In Vivo* | Y] | Y] |
| **ENVIRONMENTAL** | | |
| Bioaccumulation | Y] | N |
| Bioconcentration | Y][15] | N |
| Oct/water Part. Coeff. | Y] | N |
| Acute Fish | N | N |
| Acute Daphnia | N | N |
| Subchronic Fish | N | N |
| Subchronic Daphnia | N | N |
| Chronic Fish | N | N |
| **AVIAN** | | |
| Acute | N | N |
| Reproductive | N | N |
| Reproductive | N | N |

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[9] Guide at pp-2122. Includes new detailed criteria regarding statistical treatment, specific observations and the §8(e)-significance of maternal toxicity.

[10] Guide at pp-23; 33-34.

[11] 43 Fed Reg at 11112
Only the term "Cancer" listed.

[12] Guide at pp-21. Includes new criteria regarding biological significance and statistical treatment.

[13] 43 Fed Reg at 11112; 11115 at Comment 15
"Mutagenicity" listed/ *in vivo* vs *invitro* discussed; discussion of "Ames test".

[14] Guide at pp-23.

[15] 43 Fed Reg at 11112; 11115 at Comment 16.

# Attachment 2

## Study Summary and Report

CAS #354-64-3
Chem: (1) Perfluoroethyl iodide (pentafluoroethyl iodine, $C_2F_5I$) distilled, 98% pure (2) Perfluoroethyl iodide (pentafluoroethyl iodide,$C_2F_5I$) recycle tank, 81.8% pure
Title: Cardiac Sensitization Study
Date 7-19-77
Summary of Effects: Cardiac sensitization

Copies to: C. W. Maynard, Jr., Chambers Works (6)
R. E. Parsons, Chambers Works (1)

E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine

HASKELL LABORATORY REPORT NO. 545-77 MR NO. 2654

| Material Tested | Haskell No. | Other Codes | Material Ready for Testing | Submitted by |
|---|---|---|---|---|
| Perfluoroethyl iodide (pentafluoroethyl iodide, $C_2F_5I$) distilled, 98% pure | 11047 | OCNB 4670-150A | 2/23/77 | R. E. Parsons Jackson Laboratory |
| Perfluoroethyl iodide (pentafluoroethyl iodide, $C_2F_5I$) recycle tank, 81.8% pure | 11046 | OCNB 4670-150B | 2/23/77 | R. E. Parsons Jackson Laboratory |

Introduction: Previous testing of perfluoroethyl iodide (PFEI) indicated it was a strong cardiac sensitizer (HLR 55-73). However, since the sample tested on that study was several years old and contained an unknown impurity (1.2%), the present study was undertaken to verify those results with fresh samples. Both undistilled (H-11046) and distilled (H-11047) material were tested.

Procedure: The test animals were healthy adult male beagle dogs. A modified lead I electrocardiogram was continuously recorded throughout the experiment. The animals received a control intravenous injection of 8 μg of epinephrine per kilogram of body weight (given in nine seconds) five minutes prior to exposure; a second identical injection (challenge) was given at five minutes into exposure. Exposure was continued for five minutes after the challenge to observe recovery.

Both test samples were in pressurized cylinders and delivered through flow meters into a metered airstream. Air samples were taken every minute during exposure from a point immediately upstream from the dog's mask for gas chromatographic analysis. The reported analytical exposure concentrations are based on total test material content of the sample. The PFEI content is calculated.

Results: The results are given in the table. The criterion for a "marked response" was the development of an arrhythmia after the challenge injection of epinephrine which was not seen on the control and was considered to pose a serious threat to life (multiple consecutive ventricular beats or ventricular fibrillation).

In this study all marked responses were multiple consecutive ventricular beats. With the distilled sample (H-11047) cardiac sensitization occurred at concentrations of 500 ppm or more (see table). Twenty percent of the test animals had marked responses at 500 ppm. This is comparable to the previous study's results (HLR 55-73) in which 17% of the animals had marked responses at 500 ppm.

There were somewhat fewer marked responses with the undistilled sample (H-11046)--one of ten at 500 ppm and four of ten at 1000 ppm. Since the one "marked" response at 500 ppm was borderline (three multiple ventricular beats) and since there were no marked responses at 250 ppm with the distilled sample (which contained more PFEI) this sample (H-11046) was not tested at 250 ppm. Note that this undistilled sample had less of the major active ingredient (only 81.8% PFEI). Its impurities were perfluorinated carbons ($C_4F_{10}$ and $C_6F_{14}$) and longer chain perfluoroalkyl iodides ($C_4F_9I$ and $C_6F_{13}I$). Both perfluorocarbons and longer chain perfluoroalkyl iodides have lower cardiac sensitizing potential than PFEI (see HLR-150-72 and 66-76).

Summary: According to the conditions of this study both distilled and undistilled PFEI produced cardiac sensitization at concentrations of 500 ppm or more and are classified as strong cardiac sensitizers. The distilled sample was slightly more potent.

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Report by: Linda S. Mullin

Linda S. Mullin
Physiologist

Approved by: N. Krivanek

Neil Krivanek
Chief, Physiology Section

NB E-0571, pp. 63-68, E-3295, pp. 130-135
LSM/jtd
Date: July 19, 1977
Report No. 545-77

TABLE

Results - Cardiac Sensitization - PFEI

| Compound | Concentration Total Sample (ppm) | Concentration PFEI (ppm)* | Number of Dog Exposures | Number of Marked Responses | Percent Marked Responses |
|---|---|---|---|---|---|
| Distilled PFEI (H-11047) | 254 ± 17** | 249 ± 17 | 10 | 0 | 0 |
| | 526 ± 28 | 516 ± 28 | 10 | 2 | 20 |
| | 1033 ± 14 | 1012 ± 14 | 3 | 3 | 100 |
| Recycle Tank PFEI (H-11046) | 506 ± 17 | 414 ± 14 | 10 | 1 | 10 |
| | 1013 ± 18 | 829 ± 14 | 10 | 4 | 40 |

* Calculated

** Concentration ± one standard deviation

# Triage of 8(e) Submissions

Date sent to triage: 2/5/96

NON-CAP (CAP)

Submission number: 12146A

TSCA Inventory: (Y) N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX (SEN) w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

| | | | | |
|---|---|---|---|---|
| STOX | CTOX | EPI | RTOX | GTOX |
| STOX/ONCO | CTOX/ONCO | IMMUNO | CYTO | NEUR |

Other (FATE, EXPO, MET, etc.): _____

Notes:

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**Notes:**

**Contractor reviewer :** PDR **Date:** 5/11/95

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CECATS DATA:
Submission # 8EHQ- 1092-12146 SEQ. A

TYPE: (INT.) SUPP FLWP

SUBMITTER NAME: E. I. Dupont de Nemours and Company

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)
DISPOSITION:
(0539) REFER TO CHEMICAL SCREENING
(0678) CAP NOTICE

VOLUNTARY ACTIONS
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/OTHERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 08/10/92 OTS DATE: 10/27/92 CSRAD DATE: 03/31/95

CHEMICAL NAME:

CAS#
354-64-3

| INFORMATION TYPE: | | P F C | INFORMATION TYPE: | | P F C | INFORMATION TYPE: | | P F C |
|---|---|---|---|---|---|---|---|---|
| 0201 | ONCO (HUMAN) | 01 02 04 | 0216 | EPI/CLIN | 01 02 04 | 0241 | IMMUNO (ANIMAL) | 01 02 04 |
| 0202 | ONCO (ANIMAL) | 01 02 04 | 0217 | HUMAN EXPOS (PROD CONTAM) | 01 02 04 | 0242 | IMMUNO (HUMAN) | 01 02 04 |
| 0203 | CELL TRANS (IN VITRO) | 01 02 04 | 0218 | HUMAN EXPOS (ACCIDENTAL) | 01 02 04 | 0243 | CHEM/PHYS PROP | 01 02 04 |
| 0204 | MUTA (IN VITRO) | 01 02 04 | 0219 | HUMAN EXPOS (MONITORING) | 01 02 04 | 0244 | CLASTO (IN VITRO) | 01 02 04 |
| 0205 | MUTA (IN VIVO) | 01 02 04 | 0220 | ECO/AQUA TOX | 01 02 04 | 0245 | CLASTO (ANIMAL) | 01 02 04 |
| 0206 | REPRO/TERATO (HUMAN) | 01 02 04 | 0221 | ENV. OCCC/REL/FATE | 01 02 04 | 0246 | CLASTO (HUMAN) | 01 02 04 |
| 0207 | REPRO/TERATO (ANIMAL) | 01 02 04 | 0222 | EMER INCI OF ENV CONTAM | 01 02 04 | 0247 | DNA DAM/REPAIR | 01 02 04 |
| 0208 | NEURO (HUMAN) | 01 02 04 | 0223 | RESPONSE REQRST DELAY | 01 02 04 | 0248 | PROD/USE/PROC | 01 02 04 |
| 0209 | NEURO (ANIMAL) | 01 02 04 | 0224 | PROD/COMP/CHEM ID | 01 02 04 | 0251 | MSDS | 01 02 04 |
| 0210 | ACUTE TOX. (HUMAN) | 01 02 04 | 0225 | REPORTING RATIONALE | 01 02 04 | 0299 | OTHER | 01 02 04 |
| 0211 | CHR. TOX. (HUMAN) | 01 02 04 | 0226 | CONFIDENTIAL | 01 02 04 | | | |
| 0212 | ACUTE TOX. (ANIMAL) | 01 02 04 | 0227 | ALLERG (HUMAN) | 01 02 04 | | | |
| 0213 | SUB ACUTE TOX (ANIMAL) | 01 02 04 | (0228) | ALLERG (ANIMAL) | 01 02 04 | | | |
| 0214 | SUB CHRONIC TOX (ANIMAL) | 01 02 04 | 0239 | METAB/PHARMACO (ANIMAL) | 01 02 04 | | | |
| 0215 | CHRONIC TOX (ANIMAL) | 01 02 04 | 0240 | METAB/PHARMACO (HUMAN) | 01 02 04 | | | |

TRIAGE DATE: CAS SR

NON-CBI INVENTORY
(YES)
NO
IN INVENTORY

ONGOING REVIEW
YES (DROP/REFER)
NO (CONTINUE)
REFER

SPECIES
DOG

TOXICOLOGICAL CONCERN:
(LOW)
MED
HIGH

USE:

PRODUCTION:

COMMENTS:

12146A

Distilled PFEI: Cardiac sensitization in dogs is of ~~low~~ medium concern. Male beagle dogs were challenged with epinephrine during exposure to 249, 516, and 1,012 ppm of the test substance. Multiple ventricular beats were noted in 2/10 dogs at 516 ppm and 3/3 dogs at 1,012 ppm.

Recycle Tank PFEI: Cardiac sensitization in dogs is of ~~low~~ medium concern. Male beagle dogs were challenged with epinephrine during exposure to 414 and 829 ppm of the test substance. Multiple ventricular beats were noted in 1/10 dogs at 414 ppm and 4/10 dogs at 829 ppm.